Exhibit 12

IN THE UNITED STATES DISTRICT COURT
FOR THE EASTERN DISTRICT OF MICHIGAN

UNITED STATES OF AMERICA	)
	)
	)
Plaintiff,	)
	)
v.	)
	)
DTE ENERGY COMPANY, and DETROIT EDISON COMPANY	)
	)
	)
Defendants.	)
	)

DECLARATION OF
JOEL SCHWARTZ

1. I am a Professor in the Departments of Environmental Health and Epidemiology at the Harvard School of Public Health, in the Department of Medicine at Harvard Medical School, Director of the Harvard Center for Risk Analysis, member of the faculty of the Environmental Biostatistics program, of the cardiovascular epidemiology program, and on the Steering Committee of the Harvard University Center for the Environment. I am also a former member of the board of Councilors of the International Society for Environmental Epidemiology, and on the Editorial Board of the American Journal of Respiratory and Critical Care Medicine. I have served on two National Academy of Sciences panels, and was a recipient of a John D. and Catherine T. MacArthur Fellowship. I am the most cited author in the field of air pollution research. I have over 416 peer reviewed papers published or in press, which have been cited over 21,000 times in other peer reviewed publications. Over 200 of these scientific papers have examined particulate air pollution. I have made particulate air pollution and ground-level ozone (smog) a major focus of my research which ranges from time series studies to cohort

studies to genetic studies, and from studies focused on critical events (e.g. deaths, heart attacks) to studies addressing mechanisms and exposure. I have testified before Congress twice about particulate air pollution and testified as an expert in the health effects of air pollution in federal court.

I. SUMMARY OF CONCLUSIONS

2. Particulate air pollution from combustion is created in two ways. First, combustion processes produce particles directly, such as the soot coming off of a fire. In addition, many of the gases that are emitted by combustion, such as SO_2 and NO_x react in the atmosphere and produce particles. These are sometimes called secondary particles, as they left the source as a gas. In addition NO_x reacts with hydrocarbons in the atmosphere to produce ozone. Hence emissions of SO_2 and NO_X from coal burning power plants are major sources of particles and ozone in the air people breathe.

3. There is clear, convincing evidence that this particulate air pollution is not merely a nuisance darkening our skies. It kills people. And the number of people it kills each year in the United States is not small—it is larger than the number of deaths each year from AIDS, breast cancer, and prostate cancer put together. Hence even a fraction of a percent change in this number would be more people than die in a major airplane crash.

4. In addition to killing people, particles trigger heart attacks, destabilize people with heart failure, driving them into the hospital, and exacerbate respiratory infections, leading to increased hospital admissions for those conditions.

5. These patterns are not due to failure to exclude other possible explanations. Similar associations are seen when we control for other pollutants and weather, when we control

for pre-existing disease, smoking, etc. Moreover, animal and toxicologic studies show changes in intermediary endpoints (e.g. electrocardiogram patterns, measures of inflammation, blood pressure) that are consistent with the changes seen in the epidemiologic studies.

6. Further, studies have demonstrated down to the lowest measured exposure that these effects do not have a threshold, and that the deaths produced by particles are not just being advanced by a few weeks, but can reduce the life expectancy of entire populations by several years.

7. All of this indicates that any increase in particle concentrations has substantial effects on human health, including resulting in early deaths. Details justifying these conclusions are below. I start with mortality, and move on to other serious health effects such as heart attacks, hospital admissions, etc.

8. In this case, I was asked to assume that additional pollution controls at Monroe Unit 2 would reduce emissions by 26,525 tons of SO2 and 7942 tons of NOX per year. Based on my research, I estimate that reducing emissions by that amount would result in 90 fewer premature deaths per year and benefit to society worth approximately $542 million per annum.

9. A collection of sources supporting this discussion are listed in Attachment B. I am being compensated at a rate of $197 per hour for my work on this matter.

II. BACKGROUND ON ENVIRONMENTAL EXPOSURE-HEALTH STUDIES

10. The effects of exposures to environmental agents are generally studied using three types of studies. In toxicological studies, animals are exposed to high doses of the toxic agent, to see what responses are elicited. In controlled human exposure chambers, volunteers, usually

healthy individuals, are exposed to high doses of the toxic agents. Finally, epidemiology studies examine the species of interest at the exposures of interest.

11. The case of airborne particles is one where epidemiology particularly takes precedence. First, the effect of air pollutants can be quite different at high doses. Moreover particles seem to increase oxidative compounds in the body, putting a burden on the antioxidant defenses of the body. These differ by species. Rodents, for example, manufacture vitamin C, whereas humans require dietary intake. Second, the serious impacts of particles (and other air pollutants) seem concentrated in certain susceptible populations, such as diabetics, persons with heart disease, etc., making it very difficult to put such people in controlled exposure chambers. Finally, particles are a complex mixture, with, for example, toxic metals deposited on top of ammonium sulfate cores, pieces of soot particles stuck together, etc. Laboratory generated particles rarely have any relevance for real life particles, and laboratory animals are rarely representative of the diseases conveying susceptibility.

12. In an epidemiology study, one examines whether variations among people in their exposure are predictive of variations among people in their health. Because one can examine the full population, it is easy to incorporate persons with genetic profiles or medical conditions that make them vulnerable. Also, because air pollution is usually measured continuously, one does not have to decide in advance what the appropriate averaging time is for exposure. That is, one does not need to decide in advance to expose people to 1 hour, 2 hours, or 6 hours of exposure. One can determine it in the study. And if it is 24 or 48 hours of exposure that is the most relevant, exposure chambers are not feasible at all.

13. Toxicology studies and human exposure studies are valuable because, despite the limitations above, they provide insight into mechanisms by which exposure, in our case to

particles, produces biological effects. Overall, there have been thousands of studies of the health effects of particles in the last two decades, and the overwhelming scientific consensus is that there is no doubt that they are associated with early deaths, as well as a range of other adverse events. These studies began years ago, and over time the metric by which airborne particles are measured has changed. In the late 1980's EPA measured particles as PM_{10}, particles less than 10 micrometers in diameter. This is small enough to get down peoples' throats and into the lungs. Since the late 1990's EPA has measured (and regulated) both PM_{10} and $PM_{2.5}$, which is particles less than 2.5 micrometers in diameter. The $PM_{2.5}$ subset of PM_{10} is thought be more toxic, because combustion particles are all found in that size range, and it is more likely to deposit deeper in the lung. In urban areas in the U.S., 70-90% of PM_{10} is usually $PM_{2.5}$, so studies of PM_{10} are quite relevant for $PM_{2.5}$ health effects.

14. Below, I first summarize the overwhelming scientific consensus, and then summarize my conclusions. I follow that with a more detailed explanation of the basis for my conclusions.

III. THE SCIENTIFIC CONSENSUS

15. Over the past two decades an overwhelming scientific consensus has developed about the health effects of particulate air pollution. It is widely accepted that such particles reduce life expectancy, trigger heart attacks, and have a wide range of other adverse effects on health. Several of the most reputed health organizations have noted the consensus on the health effects of particulate matter. For example, the World Health Organization, in setting a global maximum PM_{10} standard of 20 $\mu g/m^3$ in 2005, roughly equivalent to the U.S. EPA standard of 15 $\mu g/m^3$ for $PM_{2.5}$, stated:

> By reducing particulate matter pollution from 70 to 20 micrograms per cubic metre as set out in the new Guidelines, we estimate that we can cut deaths by around 15%," said Dr. Maria Neira, WHO Director of Public Health and the Environment. "By reducing air pollution levels, we can help countries to reduce the global burden of disease from respiratory infections, heart disease, and lung cancer which they otherwise would be facing.

Their press release went on to say:

> These new guidelines have been established after a worldwide consultation with more than 80 leading scientists and are based on review of thousands of recent studies from all regions of the world. As such, they present the most widely agreed and up-to-date assessment of health effects of air pollution, recommending targets for air quality at which the health risks are significantly reduced. We look forward to working with all countries to ensure these Guidelines become part of national law

and, "For example, in the European Union, the smallest particulate matter alone ($PM_{2.5}$) causes an estimated loss of statistical life expectancy of 8.6 months for the average European."

16. Earlier, in the 2002 World Health Report, WHO concluded "Particulate air pollution (i.e. particles small enough to be inhaled into the lung) is consistently and independently related to the most serious [acute and chronic health] effects, including lung cancer and other cardiopulmonary mortality."

17. A more recent review was conducted in the United States. As part of the Clean Air Act, the U.S. EPA is required to have its summary review of the science about each criteria air pollutant reviewed by an external, statutory Clean Air Science Advisory Board (CASAC). In reviewing the EPA Staff Paper the CASAC stated, "In summary, the epidemiologic evidence, supported by emerging mechanistic understanding, indicates adverse effects of $PM_{2.5}$ at current annual average levels below 15 $\mu g/m^3$." In its letter of 6/29/06, CASAC reiterated:

> The CASAC recommended changes in the annual fine-particle standard because *there is clear and convincing scientific evidence that significant adverse human-health effects occur in response to short-term and chronic particulate matter exposures at and below 15 µg/m3, the level of the current annual $PM_{2.5}$ standard*.

It goes on to say:

> Significantly, we wish to point out that the CASAC's recommendations were consistent with the mainstream scientific advice that EPA received from virtually every major medical association and public health organization that provided their input to the Agency, including the American Medical Association, the American Thoracic Society, the American Lung Association, the American Academy of Pediatrics, the American College of Cardiology, the American Heart Association, the American Cancer Society, the American Public Health Association, and the National Association of Local Boards of Health. Indeed, to our knowledge there is no science, medical or public health group that disagrees with this very important aspect of the CASAC's recommendations. EPA's recent "expert elicitation" study (Expanded Expert Judgment Assessment of the Concentration-Response Relationship Between $PM_{2.5}$ Exposure and Mortality, September 21, 2006) only lends additional support to our conclusions concerning the adverse human health effects of $PM_{2.5}$.

18. As noted above, these conclusions are supported by all the major associations of health professionals, which include as members almost all researchers on heart disease, lung disease, and cancer. In their letter to the EPA administrator on the $PM_{2.5}$ standard the health professional organizations stated:

> There is a robust and growing body of evidence linking PM to adverse health effects. PM has now been linked to a broad range of adverse health effects, both respiratory and cardiovascular, in epidemiological and toxicological research. Epidemiological research has shown an association between PM exposure and increased risk for mortality. Time-series studies reported in the early 1990s showed that day-to-day variation in PM concentration was associated with mortality counts. These studies in selected cities have now been followed by national-level time-series analyses in the United States and Europe that pool data from broad regions to produce national estimates of the effect of PM on daily mortality.
>
> For example, in 90 U.S. cities, the National Morbidity and Mortality Air Pollution Study (NMMAPS) estimated a 0.2% increase of all-cause mortality per 10 $\mu g/m^3$ increase in PM_{10}. Risk was highest in the northeast and for cardiovascular and respiratory causes of death. Findings of follow-up studies, including most notably the Harvard Six Cities Study and the American Cancer Society's Cancer Prevention (CPS) II Study, show that the resulting loss of life may be substantial. The time-series studies show a linear relationship between PM concentration and risk at concentrations measured routinely in many U.S. cities.
>
> There is a now a substantial, parallel literature on PM and morbidity. Studies have addressed PM and risk for hospitalization and other clinical outcomes and pre-clinical

biomarkers. Since the 1997 PM NAAQS, there has been an explosion of research on cardiovascular consequences of exposure to PM indicating short-term and long-term effects of PM on cardiovascular health.

A recent study, that includes data from over 11 million Medicare beneficiaries, shows that even small increases in exposure to PM results in increased admissions for cardiac and respiratory conditions, including heart and vascular diseases, heart failure, chronic obstructive pulmonary disease and respiratory infections. The effect was even greater in participants over 75 years old, in terms of heart problems and COPD than participants 65 – 74 years old.

In short, a significant body of research has described potential mechanisms for and the range of health effects caused by PM air pollution. The undersign physician organizations find the body of scientific evidence to be rigorous, comprehensive and compelling enough to justify a significant tightening of the existing NAAQS PM standards.

Sincerely,

American Thoracic Society

American Academy of Pediatrics

American College of Cardiology

American Association of Cardiovascular and Pulmonary Rehabilitation

National Association for the Medical Direction of Respiratory Care

19. In separate comments, the *American Medical Association* wrote:

The new evidence on harmful effects of PM is substantial. PM has been linked to a broad range of adverse health effects, both respiratory and cardiovascular, in epidemiologic and toxicologic research. Studies of daily variation in concentrations and national level time-series analyses have linked PM with increased morbidity and mortality. Many U.S. and Canadian studies are available that provide evidence of associations between $PM_{2.5}$ and serious health effects in areas with air quality at and above the level of the 1997 annual standard (15 μg/m3). Newer short term mortality studies provide evidence of statistically significant associations with $PM_{2.5}$ in areas with long-term average concentrations of 13 to 14 $\mu g/m^3$, concentrations that are below the 1997 standard. Short-term studies of emergency room visits and cardiovascular mortality suggest measurable health effects at $PM_{2.5}$ concentrations of ~12 $\mu g/m^3$. A recent study (Dominici F, Peng D, Bell ML et al. *JAMA*; 2006; 295:1127-1134) showed that $PM_{2.5}$ concentrations are associated with short-term increases in hospital admissions for cardiovascular and respiratory diseases among Medicare enrollees, arguing for setting a $PM_{2.5}$ standard that is adequate to protect the health of these individuals. The AMA supports the recommendations of EPA staff and the Clean Air Scientific Advisory Committee to EPA for more stringent air quality standards. In fact, several physician organizations, including the American Thoracic Society, American College of Cardiology, American College of Preventive Medicine, and the American Academy of Pediatrics, support a more stringent $PM_{2.5}$ standard of 12 $\mu g/m^3$ for

> the average annual standard; 25 μg/m^3 for the 24-hour standard; and use of the 99th percentile form for compliance determination. The AMA believes the Administrator should adopt these more stringent standards in order to provide adequate protection for the public from the adverse health effects of both long- and short-term exposures to fine particulate matter in the ambient air.

20. Hence every major scientific body involved in either research or the evaluation of research relating to particulate air pollution has concluded that it is a major health hazard, whose consequences include early deaths.

21. The American Heart Association recently published a new review in 2010 of the impact of particles on cardiovascular health in Circulation, the world's leading peer reviewed journal on heart disease. The abstract of that peer reviewed paper summarizes the conclusions as follows:

> In 2004, the first American Heart Association scientific statement on "Air Pollution and Cardiovascular Disease" concluded that exposure to particulate matter (PM) air pollution contributes to cardiovascular morbidity and mortality. In the interim, numerous studies have expanded our understanding of this association and further elucidated the physiological and molecular mechanisms involved. The main objective of this updated American Heart Association scientific statement is to provide a comprehensive review of the new evidence linking PM exposure with cardiovascular disease, with a specific focus on highlighting the clinical implications for researchers and healthcare providers. The writing group also sought to provide expert consensus opinions on many aspects of the current state of science and updated suggestions for areas of future research. On the basis of the findings of this review, several new conclusions were reached, including the following: Exposure to PM □2.5 μm in diameter (PM2.5) over a few hours to weeks can trigger cardiovascular disease–related mortality and nonfatal events; longer-term exposure (eg, a few years) increases the risk for cardiovascular mortality to an even greater extent than exposures over a few days and reduces life expectancy within more highly exposed segments of the population by several months to a few years; reductions in PM levels are associated with decreases in cardiovascular mortality within a time frame as short as a few years; and many credible pathological mechanisms have been elucidated that lend biological plausibility to these findings. It is the opinion of the writing group that the overall evidence is consistent with a causal relationship between PM2.5 exposure and cardiovascular morbidity and mortality. This body of evidence has grown and been strengthened substantially since the first American Heart Association scientific statement was published. Finally, PM2.5 exposure is deemed a modifiable factor that contributes to cardiovascular morbidity and mortality.

22. The US EPA has recently prepared a new Integrated Science Assessment summarizing the state of the science about particulate air pollution, which has been reviewed by the Clean Air Scientific Advisory Committee. That assessment states:

> Epidemiologic studies that examined the effect of PM2.5 on cardiovascular emergency department (ED) visits and hospital admissions (HA) reported consistent positive associations (predominantly for ischemic heart disease [IHD] and congestive heart failure [CHF]), with the majority reporting increases ranging from 0.5 to 3.4% per 10 µg/m3 increase in PM2.5. These effects were observed in study locations with mean1 24-h avg PM2.5 concentrations ranging from 7-18 µg/m3 (Section 6.2.10), with effects becoming more precise and consistently positive in locations with mean PM2.5 concentrations of 13 µg/m3 and above (Figure 2-1). Toxicological studies have provided biologically plausible mechanisms (e.g., increased right ventricular pressure and diminished cardiac contractility) for the associations observed between PM2.5 and CHF in epidemiologic studies.
> and: There is also a growing body of evidence from controlled human exposure and toxicological studies demonstrating PM2.5-induced changes on markers of systemic oxidative stress and heart rate variability (HRV) (Section 6.2.1 and Section 6.2.9). Additional, but inconsistent effects of PM2.5 on BP, blood coagulation markers, and markers of systemic inflammation have also been reported across disciplines. Together, the collective evidence from epidemiologic, controlled human exposure, and toxicological studies is sufficient to conclude that a causal relationship exists between short- term exposures to PM and cardiovascular effects.

and:

> Collectively, the studies evaluated demonstrate a wide range of respiratory responses, and although results are not fully consistent and coherent across studies the evidence is sufficient to conclude that a causal relationship is likely to exist between short-term exposures to PM2.5 and respiratory effects.

and:

> An evaluation of the epidemiologic literature indicates consistent positive associations between short-term exposure to PM2.5 and all-cause, cardiovascular-, and respiratory-related mortality (Section 6.5.2.2.). ....Collectively, the epidemiologic literature provides evidence that a causal relationship is likely to exist between short-term exposures to PM2.5 and mortality.

and:

> Evidence from toxicological studies provides biological plausibility and coherence with studies of short-term exposure and CVD morbidity and mortality, as well as with studies that examined long- term exposure to PM2.5 and CVD mortality. Taken together, the evidence from epidemiologic and toxicological studies is sufficient to conclude that **a**

> **causal relationship exists between long-term exposures to PM2.5 and cardiovascular effects.** (emphasis in original)

(Integrated Science Assessment for Particulate Matter. Second External Review Draft. ISA: EPA/600/R-08/139B).

Commenting on the ISA, the CASAC, EPA's Statutorily mandated external science advisory committee stated, "CASAC also supports EPA's changes to the causal determinations for long-term exposure to PM2.5 and cardiovascular effects (from 'likely causal' to 'causal') and, "CASAC recommends 'upgrading' the causal classification for PM2.5 and total mortality to 'causal' for both the short-term and long-term time frames" (EPA-CASAC-10-001 Letter to the Administrator). That is, CASAC has concluded that the association between PM2.5 and deaths is causal.

IV. PARTICLES AND MORTALITY

23. Several different types of studies have been used to examine the relationship between particles and mortality: long term exposure studies have focused on the association between longer term exposure to particles and life expectancy, whereas other studies have looked at the acute responses within a few days of exposure. Finally, there are some intermediary studies that attempt to bridge the gap. Within studies of longer term exposure there are further distinctions based on whether the exposure contrast is just between cities, or whether it includes, or is limited to, contrasts within a metropolitan area. Also, some studies incorporate changes over time in exposure**.** I discuss these various types of studies below.

IV.a. Long Term Exposure Studies

Mortality

24. I find, as did the major scientific organizations, that there is clear, convincing evidence that exposure to particles shortens life expectancy by substantial amounts. I base this judgment on the extensive literature, as outlined below.

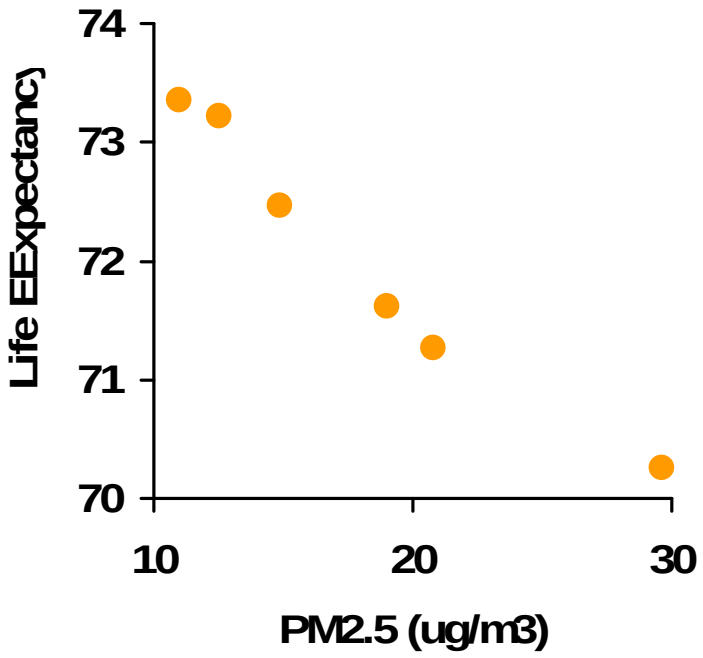
25. In 1970, Lave and Seskin published a paper regressing age standardized mortality rates in US cities against average particle concentrations in those cities. The advantage of that study was that the mortality experience of the entire population of each city was compared to the average particle concentration from the population- oriented monitors in the city. The difficulty was that no individual level covariates (i.e. other individual factors such as hypertension, diabetes, smoking, etc that may differ on average between the people in different cities, and might explain the differences between those cities in mortality rates) were controlled, raising questions about confounding (i.e. that another variable explains the observed association).

26. More recent studies have alleviated that problem by recruiting cohorts of individuals in various areas, and measuring those individual covariates. An issue with most of those cohort studies is that they are convenience samples, and unlike Lave and Seskin, do not capture the typical mortality experience or the typical exposure of the population of the city they live in. If the convenience sample differed in health and exposure from the population average similarly in all locations, this would ameliorate the problem. However, we cannot be sure this is true. Specifically, the American Cancer Society (ACS) cohort was recruited from friends of the volunteers of the society. The ACS volunteers in city A may represent a healthier, and less exposed subset of city A then they do in city B.

27. This is problematic for two reasons. First there is potential confounding. If, for example, the cities with higher exposures had **systematically** less healthy subjects recruited, this would tend to enhance the size of the air pollution effect. If they **systematically** had more healthy subjects, it would attenuate the size of the air pollution effect. I know of no reason to assume that either is true. Most people are unaware of the relative pollution level in their town, and hence this is unlikely to effect volunteering for the American Cancer Society—I would expect such differences to occur by chance, and, on average, not be related to pollution levels. However, there undoubtedly are some random fluctuations in the relative health and relative exposure of the subjects from city to city. This is likely to lead to an underestimate of the effect of exposure on mortality risk, which is the general result of such non-differential measurement error. Moreover, studies where the relation between sample health and population health varies more substantially from city to city have a greater risk of this additional uncertainty and potential bias.

28. These concerns apply to all of the cohort studies, with the obvious exception of the Six City Study. The Six City Study chose a neighborhood within each city, recruited a **random** sample of that neighborhood, and put a population oriented particle monitor in the middle of each neighborhood. Most subjects lived within a few kilometers of that central monitor, and the exposure error was much lower than in studies using the average of all monitors in a greater metropolitan area. Further, bias due to differential sampling in different locations was eliminated by the random sampling. This means that the extra source of uncertainty, and extra downward bias, present in the other studies is not present in the Six City Analysis, suggesting this study should be given greater consideration. The reduction in life expectancy with higher exposure to particles that the Six City Study found was substantial, as indicated in

the figure below, which shows the life expectancy in each city, after adjusting for age, sex, cigarette smoking, occupation, education, obesity, and chronic disease, plotted against the mean $PM_{2.5}$ in that city. To put this in perspective, between 1995 and 2005 life expectancy in the U.S. increased by 2 years. Hence, PM can obliterate the effects of one and a half decades of medical progress on life expectancy.



29. Further evidence that the original ACS study (among others) underestimated the effects of particles on deaths comes from a recent reanalysis of the ACS study that only used monitors in the same county of residence of each subject to assign exposure (the original could assign subjects exposure from a monitor in a different county on the opposite side of the metropolitan area). That study found a higher coefficient for the effects of sulfate particles on mortality than the original study. Even more intriguingly, a recent study examined only the

22,905 participants of the ACS study living in Southern California using a geographic information system based exposure model, which captures the local exposure gradient within Southern California, and reported even larger effect size estimates for $PM_{2.5}$. Similarly, the Women's Health Initiative study found a larger effect on mortality when they used within-city exposure estimates. Hence the use of more localized measures of exposure, with resultant lower exposure error, generally has resulted in larger effect estimates.

30. Studies that examine change in exposure play an important role in understanding the effects of particles for several reasons. First, if particle-induced changes in health are permanent, and we have to wait for a new generation before seeing public health improvements follow the exposure reductions, there are important public health implications. It certainly dramatically affects any cost-benefit analyses. Secondly, showing that a change in exposure produces a change in response more directly addresses the causality of the association. If A causes B, then changing A will change B. Finally, cross-area comparisons between lung function, mortality rates, or any other response and cross-area variations in exposure across communities have the potential to be confounded by any unmeasured predictors of outcome that vary geographically (by confounder I mean another variable (e.g. hypertension) that is causally related to the outcome, and correlated with exposure, which actually explains the observed association between, in our case, particles and outcome). That is, if we controlled for that other variable the association with particles would go away.

31. Naturally, epidemiology studies try to identify such variables and control for them. Equally importantly, the Six City Study went further, and showed the association of air pollution with life expectancy before and after controlling for each potential confounder, such as smoking, hypertension, diabetes, occupational exposures, obesity, etc. There was no evidence of

confounding by any of the covariates examined except age. This provides some reassurance that confounding is unlikely. However, one cannot measure everything about a person's health, so it is always possible that such confounding exists. That is why it is important to look at multiple studies, and multiple study designs that have different potentials for such confounding. For example, unless we think that air pollution increases hypertension, in our example above, then there should not be any systematic correlation between air pollution levels in a city and the rate of hypertension. However, by chance, such a correlation may have occurred in one particular study limited to one set of locations. A different study in a different set of locations is less likely to have that confounding. And even if hypertension were systematically associated with higher air pollution in the U.S., perhaps because of the clustering of some behavior patterns in regions of the country that happen to be more polluted, why would that confounding remain if we only looked at differences in exposure and differences in mortality risk **within** a city, as in the new ACS analysis or the Women's Health Initiative analysis? And if there was something about the U.S. social structure that made that true in U.S. cities, why would that still be true in the Netherlands, with a very different social structure, where within city variations in particles were also associated with variations in the risk of death? Of course, all the cohort studies mentioned did control for hypertension, but there may be other unmeasured factors that are potential confounders in any one of them. The same arguments above apply—it is hard to see how those same unmeasured confounders could apply in all the cases above.

32. One other way to assure that the observed association is real is to conduct studies not merely in different locations, and across different scales of geography, but in different ways, including where exposure varies by time, and not geographic location. Examinations of year to year changes in exposure within location do not suffer the potential confounding that, as above,

some unmeasured confounder may differ from one city to another. Other variables, which do vary from year-to-year, might confound, but are unlikely to be correlated with the potential confounders of the cross-sectional associations. Hence, if associations are seen using this very different study design as well, it provides greater confidence that the associations are causal.

33. Consequently a key finding for cohort studies of mortality has come from studies examining changes in exposure and changes in mortality rates. Most of the cohort studies, including the original Six City Study, have contrasted a measure of long-term exposure with long term survival. They tell us that people live less long in more polluted cities. They do not, directly, tell us what mortality reduction accompanies a reduction in exposure. In a follow-up of the Harvard Six City Study, Laden and coworkers provide precisely that estimate. They examined a further 10 years of follow-up and mortality in the six cities. In some cities there was a substantial drop in pollution between the first and second follow-up periods, in some cities there was a moderate drop, and in some cities there was little or no change. The mortality rate ratios followed the same pattern: where there was a substantial drop in pollution there was a substantial improvement in life expectancy; where there was little change in pollution concentrations there was little change in life expectancy. The slope for change in exposure was similar to, but slightly higher, than the cross-sectional slope.

34. Again, if the mortality rates change within a town as the air pollution changes, and those changes fit on the same dose-response curve as the original cross-sectional association, this provides substantial assurance that the association is not confounded, because the factors that are likely to confound an association of temporal change are usually different from those that might confound a cross-sectional study, and there is no reason for the confounding of two different estimates by different confounders to produce similar estimated effects for particles.

35. Another follow-up analysis of the Six City Study looked at year-to-year changes in particle concentrations to examine two questions—does the dose-response continue below 15 $\mu g/m^3$; and what is the lag between change in exposure and change in mortality rate. Schwartz and coworkers, using a penalized spline with up to 18 degrees of freedom (essentially, a polynomial with 18 terms to capture any deviation from linearity), showed that the association was essentially linear down to 8 $\mu g/m^3$, where the data becomes sparse, and that the effects of reduced particle exposure on mortality appear to be mostly seen within two years. This conclusion is also supported by natural experiments. Pope and coworkers reported that mortality fell in the Utah valley in the year a strike closed a steel mill, and returned to its previous level the next year when mill operations resumed.

36. Because the uncertainties around the dose-response curve from fitting a particular model do not reflect the uncertainty in model choice we also used model averaging, where 32 models are fit explicitly, and averaged, weighted by their probability of being correct given the data. These models explicitly included the possibility of thresholds at multiple different particle concentrations. The association was indistinguishable from linear with no evidence of a threshold down to the lowest measured level of 8 $\mu g/m^3$. The finding of a rapid change in mortality risk associated with change in particle exposure in the Six City Study fits nicely with the similar report for lung function from the Swiss Cohort Study on Air Pollution and Lung Diseases in Adults (SAPALDIA) study.

37. Another recent study examined changes in life expectancy across 51 metropolitan areas in the United States, between 1980 and 2000. They found that 15% of the *increase* in life expectancy during that period came from *decreases* in air pollution, and that in the more polluted cities that cleaned up, life expectancy was increased by 10 months.

38. Recently, the study of Zanobetti and Schwartz examined over 190,000 subjects discharged alive from hospitals following myocardial infarctions (heart attacks). They looked at year to year changes in exposure **within** cities related to the probability of surviving that year, given the participant was alive on January 1. They adjusted for long term time trend, and did separate analyses within each of 21 cities. They then combined the results across cities. This approach does not allow any differences in exposure across a city to contribute to the association (which is only examined *within* the city), and again focuses on temporal changes in particles and mortality. Hence, as in the Six City analysis above, the set of potential confounders is quite different from those in a traditional cohort study. They reported a significant association with PM_{10} in this susceptible subgroup; they also found larger coefficients (the slope between exposure and mortality risk) than were seen in the Six City Study. A follow-up study looking at people with chronic bronchitis and emphysema in the same manner found a similar result. Another study in a similar vein was the work of Janke and coworkers. They looked at 354 local governmental units in England. They look at annual mortality rates for multiple years in each location, controlling for *location and local time trend*. In effect they are looking at whether random deviations from year to year in air pollution around the local means and local time trend are correlated with random deviations in mortality rates around the local mean and local time trend. Such a design leaves little room for confounding. They found a strong association with particulate air pollution.

39. Another new cohort study examined over 66,000 nurses living in the Northeast and upper Midwest. Using a spatial model that estimated monthly $PM_{2.5}$ concentrations at the addresses of each nurse, they found that a 10 $\mu g/m^3$ increase in $PM_{2.5}$ at the nurse's address was associated with a 26% increase in risk of dying in that year. Similar to my analysis of the Six

City Study, they found this increase was predominantly seen within a year of the change of exposure. This effect estimate is considerably higher than the Six City estimate, suggesting again the improved exposure results in higher estimates of the effects of particles on mortality.

40. More recently an innovative study modernized the Lave and Seskin approach. They looked at over 2300 counties in the Eastern US, and used remote satellite sensing data to estimate $PM_{2.5}$ concentrations. The satellite data allows the incorporation of the many counties without monitoring. This allowed them to include thousands of counties, rather than hundreds. They reported that standardized mortality rates for ischemic heart disease were associated with $PM_{2.5}$, in a region of the country where sulfates are a major source of $PM_{2.5}$

41. Another recent analysis, which extended the previous analyses of the ACS study to include more years and more data, importantly reported associations between sulfate particles, the type produced by coal burning power plants, and deaths from ischemic heart disease. Interestingly, they found that control for socio-economic status increased the risk associated with sulfates, rather than decreasing it.

42. This fits in quite well with developing studies looking at shorter term exposure to air pollution (discussed in the section on acute effects below), that have extended their ambit from looking at immediate effects of the last few day's exposure to include months of exposure. I examined the association of daily deaths and hospital admissions with particles when averaged over different periods, from days to months, after filtering out seasonal and long term trends. I found that the size of the PM effect increased as one went from days to periods of up to two months. At that point, the effect size estimates seemed intermediate between those reported in classical time series, which looked at yesterday's exposures, and those reported in the cohort studies.

43. As part of this approach, I developed a framework for thinking about this question. In this framework, the population is divided into a general pool, with low risk of dying, and a frail pool with high risk of dying in the near future. Because the causes of frailty can be at least partially reversible (e.g. subjects with pneumonia recover, subjects who survive a myocardial infarction have much lower risk of dying in the second month after the infarct than in the first, etc.) it is possible to transition back to the general pool from the frail pool. Meanwhile, other events can cause transitions from the general pool to the frail pool. If the effect of particles on the recruitment rate into, or retention in, the frail pool, is greater than the effects of particle exposure on the death rate out of the frail pool, increased exposure will result in an immediate increase in deaths (from the direct effect of particles on the death rate out of the frail pool), and also a delayed effect, as the increased population of the frail pool results in excess deaths over the next few months. The results of my studies indicate that this is the case.

44. A frequency domain regression approach by Zeger and coworkers showed similar results[22]. In several studies, Zanobetti and coworkers examined the time course of the mortality–death relationship directly, using distributed lag models. These models showed a pattern concordant with my hypothesis. There was an immediate increase in deaths following an increase in particle exposure, followed by a long tail of slightly increased deaths, stretching out for 40 days after the initial response. Time series studies by their nature have to control for season, and this makes it difficult to examine lags longer than a month or two, but the substantial increase in effect size reported by Zanobetti in these studies again suggests that the short term and long term responses to changes in airborne particles fall on a continuum.

45. Further support for this theory comes from recent studies looking at pregnancy outcomes and infant mortality. Both responses, by definition, involve exposures of less than a

year. For example, Bobak and Leon examined the cross–sectional association between air pollution and infant mortality rates across towns in the Czech Republic. A significant association was seen with particle concentrations. Woodruff and coworkers compared infant death rates in US cities with their levels of PM in the air. They excluded infant deaths in the first month after birth as likely to reflect complications of pregnancy and delivery, and found that PM_{10} was associated with higher death rates in the next 11 months of life. This excess risk seemed to be principally from respiratory illness, although sudden infant death syndrome deaths were also elevated. Further studies confirmed this association.

46. The association between airborne particles and mortality implies a very large public health impact. For example, the Laden paper suggests that an average 5 $\mu g/m^3$ decrease in $PM_{2.5}$ concentrations in the US would be associated with a 5-10% decrease in all cause mortality, which is 100,000-200,000 fewer deaths per year. **For comparison, the lower bound estimate is more deaths than from AIDS, breast cancer, and prostate cancer combined**.

Other Effects of Long Term Exposure

47. Long term exposure to particulate air pollution is not merely associated with increased risk of dying. It is associated with a wide range of other outcomes, which are in themselves consequential for health, and which also provide a coherent pattern with the mortality associations.

Lung Function

48. Lung function is one of these other outcomes that, in my judgment, is clearly affected by particles. Particles levels are associated with less growth of lung function among children and teenagers, and with faster decline of lung function in adults. This is important

because lung function is one of the best predictors of cardio-respiratory health and life expectancy, although the reasons are not completely understood. This makes associations between particulate air pollution and lung function relevant for other health outcomes. In the 1950's a study examined the lung function of British Postal workers, and found that workers in large urban areas with greater pollution consistently had lower lung function. The advantage of this study was that the postal workers generally stayed in the same counties all of their careers, and were of the same social status. Since then many other studies have reported associations between lung function and particles in the communities where people resided.

49. A recent example is the paper of Lubinski and coworkers, who reported decreases in the ratio of forced expiratory volume in one second (FEV1) to forced vital capacity (FVC), and in FEV1 as a percent of predicted associated with increased exposure to particles in nonsmoking young Polish men. While these studies looked at differences in PM exposure **between** communities, a study of the rate of lung function growth in children, using data from **within** city variations in Mexico City, reported reduced rates of growth associated with living in parts of the city with higher particle levels.

50. Again, a study that looks at differences in exposure over **time**, instead of over **space** is unlikely to be troubled by the confounders of a study looking at differences in exposure over space, and vice versa. This provides strong support for the causality of the association. A dramatic effect of such a change in exposure was seen by Avol and coworkers. They identified 110 children from the University of Southern California Children's Health Study who moved from the study area, and followed them in their new home with pulmonary function testing identical to that in the main cohort. Subjects who moved to locations with higher PM_{10} concentrations had lower rates of annual growth in lung function, while children who moved to

locations with lower PM_{10} levels than they had left showed higher rates of growth in lung function. This effect was increased in subjects who lived in the new location for at least three years.

51. A similar finding has been reported in adults. The Swiss Cohort Study on Air Pollution and Lung Diseases in Adults (SAPALDIA) is a prospective study of a random sample of adults in eight Swiss communities who were given lung function tests in 1991 and again in 2002. The initial study reported lower lung function in communities with higher particles, controlling for individual risk factors. The follow-up used sophisticated air dispersion models to estimate exposure at each person's address, accounting for any changes in address over the intervening 11 years. In analyses adjusted for town of origin, covariates, and baseline exposure, a decrease of 10 $\mu g/m^3$ in the average subject specific PM_{10} concentration between examinations was associated with a 9% decrease in the annual rate of decline in FEV_1 (i.e., by 3.1 ml/yr; 95% confidence interval (CI), 0.03 to 6.2), and a 16% decrease in the annual rate of decline in forced expiratory flow between 25% and 75% of volume out ($FEF_{25–75}$) (i.e., by 11.3 ml per second/yr; 95% CI, 4.3 to 18.2). This annual decrease in lung function is a strong predictor of survival—people whose lung function declines more rapidly as they age have a shorter life expectancy. Hence, these results are consistent with the finding that decreasing exposure results in increased life expectancy, reported earlier.

Respiratory Symptoms

52. I also find convincing evidence that long term exposure to particles is associated with increases in bronchitic symptoms, chronic cough, and other serious respiratory illnesses.

53. Dockery and coworkers, comparing symptom reports across six communities in the eastern United States with varying levels of pollution, and controlling for individual risk

factors, found that chronic bronchitis and chest illnesses in children were associated with exposure to particulate air pollution. No association was seen with asthma or wheezing.

54. Subsequent studies in the US and Europe confirmed that particle exposure across communities was associated with higher rates of chronic cough and bronchitis symptoms in children, and the lack of association with wheezing and asthma. For example, a large study (n=4,470) examined school children in 10 communities in Switzerland and reported an odds ratio for bronchitis of 2.88 (95% CI 1.69–4.89) for PM_{10} exposure between the most and least polluted community. That is, rates of bronchitis were almost 3 times as large in the highest PM community. The previously mentioned Southern-California-study examined 3,676 children across 12 communities and found that bronchitis was associated with PM_{10} , but only among children with asthma. The largest study was the Harvard-24-city-study, which examined 13,369 children. Particulate air pollution was associated with bronchitis episodes across these communities, controlling for individual risk factors.

55. Again, these studies have been complemented by studies examining **change** in pollution and **change** in symptom status. A follow-up of the Swiss children's study mentioned above reported that decreases in PM_{10} were associated with decreased respiratory symptom reporting in the 10 communities. Another recent follow-up of the SAPALDIA study reported that changes in PM_{10} exposure estimated at peoples' addresses was associated with changes in chronic respiratory symptoms during the 11 year follow-up. Similarly, declines in particle levels in East German towns following the collapse of communism were associated with declines in the rate of bronchitis and chronic cough in children.

56. Lending further credence to these reports is the study of Giroux and coworkers that contrasted exhaled NO (a marker of lung inflammation) in asthmatic children living in urban

areas with others staying in a national park in the mountains. They found the exhaled NO concentrations in the urban asthmatic children were more than double those in the asthmatic children in the national park, indicating that urban air pollution is associated with pulmonary inflammation.

57. Long term exposure to PM has also been associated with the development of chronic respiratory symptoms in adults. For example, I reported in 1993 that chronic pulmonary symptoms such as bronchitis were associated with long term exposure to air pollution in the NHANES II study adults[47]. Using data from the Seventh Day Adventist Study, a number of papers have reported associations between particle exposure and chronic respiratory symptoms, mostly recently using $PM_{2.5}$ as the exposure. Avino and coworkers also reported an association in a more limited two community study. An interesting case-control study by Karakatsani used in home examinations by physicians, including pulmonary function testing to confirm self reports of chronic respiratory conditions in adults, and in age and gender matched controls. A geographic model was used to assign individual exposure values, which were associated with the risk of chronic bronchitis and COPD.

Cognitive/neurotoxic effects

58. One of the most intriguing recent findings about particles is the report of Franco-Suglia et al. They used a geographic exposure model, calibrated to 82 different monitoring locations, to estimate the geographic variation of traffic particles in Boston (sulfate particles in Boston, coming primarily from the Midwest, are uniform in concentration across Boston, and hence could not be examined in this study). That does not mean the effects seen may not also occur with sulfate particle exposures. To date, the evidence for the toxicity of sulfate particles is as strong as for other particles. It is just that sulfate exposure was the same for all of the children

in the study, and so we could not examine the hypothesis). From this model, they estimated chronic exposure to traffic particles for school-aged children living in Boston. Higher particle exposure was associated with decrements in cognitive function of the order of 2 IQ points. Consistent with this, Rauh et al measured prenatal and post-natal exposure to ETS and Bayley Scales of infant development in 226 urban children enrolled during pregnancy and followed longitudinally. Prenatal ETS exposure (dichotomized as yes/no) predicted a 5 point decrement in the Bayley MDI scores($p=0.02$). Second hand smoke is enriched in combustion particles compared to primary tobacco exhaust, which has more gases. This is a major potential health hazard that requires confirmation. However, it does have some toxicological support.

59. Specifically, particles have been shown in experimental protocols to translocate from the nose up the olfactory nerve into the brain, with exposures shown not only in the olfactory bulb, but also in the striatum frontal cortex, and cerebellum. This in turn is associated with increased inflammatory responses in the brain, as well as changes in neurotransmitter levels. More recently, exposure to diesel exhaust has been shown to produce changes in electroencephalographic patterns in human volunteers, indicative of cortical stress. Calderon-Garciduenas and coworkers have produced a series of studies of small populations of children and dogs in Mexico City and a control, much less polluted Mexican city. They have reported that the dogs from Mexico City had greater rates of prefrontal lesions, neuroinflammation, gliosis, and particle deposition. MRI evaluation of the children's brains also revealed greater prefrontal lesions, and autopsy studies of accident victims showed upregulation of cyclooxygenase-2, ILb, and CD14 in victims living in more polluted locations.

60. Another study examined over 56,000 emergency admissions for severe Migraine attacks in Edmonton hospitals. Migraine is related to changes in brain cell receptors and neurotransmittors. Emergency visits were associated with $PM_{2.5}$ concentrations.

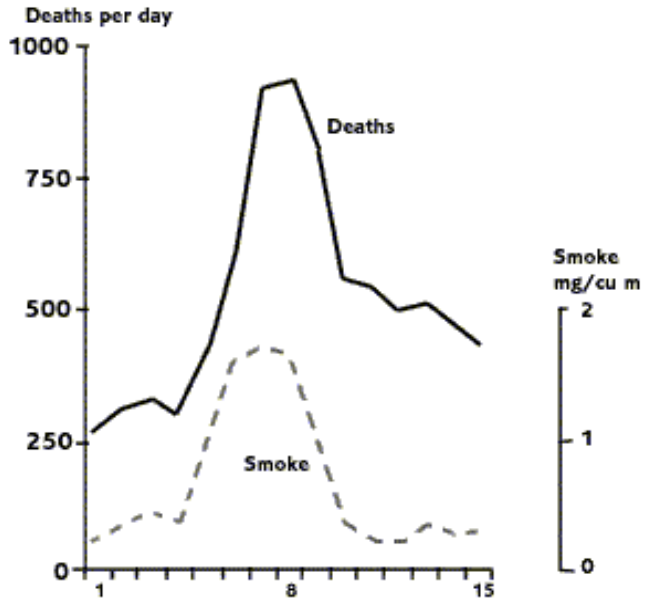
IV.b. Studies of Short Term Exposure

Mortality Studies

61. It is my opinion that airborne particles clearly are associated with increased deaths on the same and subsequent days. These results are confirmed by large numbers of studies.

62. The earliest and clearest studies of the effects of short-term changes in particles on mortality focused on severe air pollution episodes. Death counts for several days or weeks during and immediately after the episodes were compared to those before and after the event, or to the same dates in other years. These studies unambiguously showed that high concentrations of PM could increase death rates. For example, the figure below shows daily deaths and daily black smoke concentrations (produced by coal combustion) in London in the 1952 episode. As the month began a combination of weather fronts produced a sharp drop in wind speed, particularly over the southeast part of the country. On December 4 the wind velocity at the Kew Observatory in west London dropped from 6 knots at noon to 0 knots by 6pm. A low level thermal inversion combined with this to produce a rapid increase in particle concentrations. Deaths rose rapidly with the increase in particles. They also trailed off rapidly with the fall in particles, but while there was an initial rapid decline it had a slow tailing off and did not drop back to pre episode levels, but remained somewhat elevated for several weeks. This long tail of increased deaths after an episode has been reported in other episodes, and is consistent with the

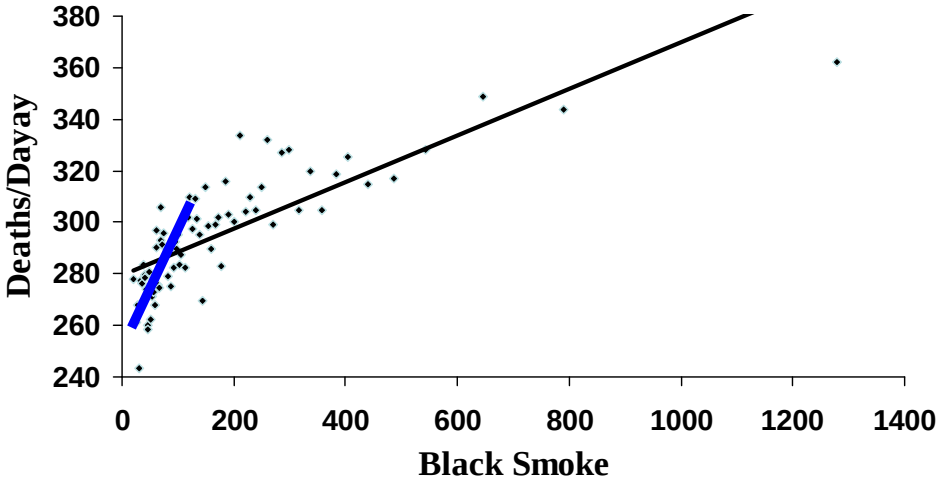
results of Zanobetti et al discussed above, where more usual particle exposure had an effect on mortality for weeks after the exposure.



63. This pattern was not due to influenza, because the epidemic did not hit Britain until about a month later. In the 160 Great Towns of England and Wales (excluding London) the weekly deaths changed from 4585 the preceding week to 4749 the week of the episode. The increase in pollution was far less in those towns, due to a lack of temperature inversions. Similar associations were reported in other episodes. By their nature, such studies do not tell us what happens at more usual exposures.

64. In the early 1990's the results of several daily time-series studies were reported[7]. These studies did not rely on extreme pollution episodes, but evaluated changes in daily mortality counts associated with daily changes in air pollution at relatively low, more common

levels of pollution. For example, the below figure shows the average deaths in London and black smoke pollution from 14 winters (1958-71), as described by Schwartz and Marcus.



65. It clearly shows the association extends to as low as the pollution measurements, and that the slope relating daily deaths to particles is steeper at lower exposure levels. This result has been confirmed multiple times. Since this time, large multi-city studies of millions of deaths have confirmed that, controlling for season and weather, when airborne particles increase, daily deaths increase. This has been found in the United States, Europe, and Asia.

Case Crossover Studies

66. The case–crossover design, introduced by Maclure in 1991, is a method for investigating the acute effects of an exposure. In the case–crossover approach, a case–control study is conducted whereby each person who had an event is matched with him/herself on a nearby time period where s/he did not have the event. The subject's characteristics and exposures

at the time of the case event are compared with those of control periods in which the event did not occur. If exposure is related to the risk of an event, then we would expect, on average, higher exposure levels on the event days than on the control days. This approach has been applied to studying mortality effects of daily changes in particulate air pollution.

67. Applied to the association of air pollution with risk of death, the approach has several advantages. Because in this analysis each subject serves as his or her own control, the use of a nearby day as the control period means that all covariates that change slowly over time, such as smoking history, age, obesity, usual diet, diabetes, and so forth, are controlled for by matching.

68. The method also allows a more straightforward approach to seasonal control. Traditional methods involve Poisson regressions with smooth functions or regression splines to control for season. The case–crossover design controls automatically for seasonal variation, time trends, and confounders that vary slowly by time because the case and control periods are separated by a relatively small interval of time. That is, season and time trends are controlled by matching. Bateson and Schwartz demonstrated that by choosing control days close to event days, even very strong confounding of exposure by seasonal patterns could be controlled by design in the case–control approach. This makes the approach an attractive alternative to the Poisson models.

69. Once one has adopted the framework of choosing control days close to the event day for each subject, it is straightforward to extend this to control for a gaseous air pollutant. One can examine all of the potential control days that are close enough in time to each event day to control for seasonal confounding, and select the subset that also matches on the level of a gaseous co-pollutant. Since the day of death and control day for each decedent have the same

concentration of the other pollutant, the association between PM and death (from having on average higher PM on the day of death than the control day) cannot be alternatively explained by the other pollutant, since it is always the same on both days.

70. I applied this approach to a study of particulate air pollution and daily deaths in 14 U.S. cities. After matching, there were about 400,000 deaths in each analysis. PM_{10} was a significant predictor of mortality when controlling for gaseous air pollutants, with effect sizes ranging from a 0.45% increase in daily deaths per 10 $\mu g/m^3$ increment of PM_{10} [95% confidence interval (CI), 0.12–0.79%] when death and control days were matched ozone levels, to a 0.81% increase per 10 $\mu g/m^3$ increment of PM_{10} (95% CI, 0.47–1.16%) when matched on SO_2.

Confounding

71. There is convincing evidence that the association of particles with early death cannot be explained by confounding. This issue is the same for the studies of acute effects of particles as it is for the effects of longer term exposure—could some other factor, correlated with both exposure and mortality, explain the observed association? As noted above, the matching of case and control days by SO_2, NO_2, CO, and O_3 unambiguously showed that particles were associated with higher daily death rates in situations where those pollutants could not possibly be alternative explanations of the observed association, because they were the same on the day of death and control day. I did a similar study where the day of death and control day was matched by temperature, and again showed there was no confounding. Hence neither temperature nor other air pollutants can explain the observed association. Other studies using different methodologies have arrived at the same conclusion. For example, the NMMAPS study fit two pollutant models in the twenty largest US cities to estimate whether there were significant

associations independent of gaseous pollutants, and found that the association with particles was unchanged by control for gases. Another approach used a two stage hierarchical model to examine confounding by gaseous air pollutants. The basic idea of this approach is that since the relationship between particles and the putative confounder varies by city and season, if the observed particle effect is really due to the other air pollutant, its size should vary in the same way as that relationship between the particles and the confounder. It did not, confirming the lack of confounding by other pollutants.

72. Another possibility considered was confounding by respiratory epidemics. To examine this, Braga and coworkers analyzed daily deaths and PM in 5 U.S. cities in two ways. First they did the now classic Poisson time series analysis. Then, they used hospitalization data for pneumonia to identify each serious respiratory epidemic in each city. They fit 6^{th} degree polynomials for each epidemic in each city to explain its rise and fall with time, and compared the association with particles to the original results. There were no changes in the association between daily PM and daily death with or without control for epidemics.

73. Another way to ensure an association is not explained by another air pollutant is to do it in a location and time where that other air pollutant is not present. For example, Fairley examined the association of particles and daily deaths in Santa Clara CA, in the winters. Since ozone is a summertime pollutant, ozone was essentially not present, and since sulfur containing fuels are not used in California, SO_2 levels were essentially non-existent. Yet similar associations with particles were seen as in other cites. Similarly, there is essentially no SO_2 in Provo Utah, where particles have been associated with daily deaths. Note that here we are talking about confounding by the direct effects of SO_2, not about its role as a precursor to sulfate particles. Similarly, the analysis of London winters could not have been confounded by ozone.

74. The recent report of Sarnat et al in Baltimore is also informative on the question of confounding. To argue that the effect of particles on mortality is really due to the fact that particle concentrations are correlated with, for example, SO_2 concentrations, makes an unspoken assumption. It assumes that particle concentrations measured at monitors in a city are related to personal exposure to particles, and that SO_2 concentrations are related to personal exposure to SO_2. Sarnat and coworkers used personal samplers that measured personal exposures to particles and these other pollutants in adults and children in the summer and winter to determine whether this was true. They found that personal exposures to particles and the particle concentrations at monitors were related. They also found that day-to-day variations in gaseous air pollutants measured at the central monitoring stations in the city **were not associated** with day-to-day changes in personal exposures to those gases. However, the monitored values of SO_2 and other gases *were* associated with day-to-day changes in personal exposure to $PM_{2.5}$. Hence, measurements of gaseous pollutants at central monitoring stations are not approximations of exposure to those gases. They are approximations of exposure to particles. In contrast, the measurements of particles at the central monitoring stations were correlated with personal exposure to particles. Hence ambient measurements of gases **may be alternative surrogates for exposures to particles and not measurements of confounders at all**. This indicates that studies of particles should not control for those gases.

75. Another recent personal exposure study examined the association between ambient measurements of temperature, personal exposure to temperature, and skin temperature in Baltimore. In this case, as well, ambient temperature was not correlated with either personal exposure to temperature or with skin temperature, indicating little potential for confounding.

This is not surprising. Adults in the U.S. spend over 95% of their time indoors, where space heating is ubiquitous and air conditioning common.

Threshold and Dose-Response

76. One special topic is whether there is a threshold in the association between PM and daily deaths. This has been addressed in a number of large multi-city studies. For example, I introduced an approach called meta-smoothing, to combine nonlinear dose-response curves across multiple studies. In simulation studies, I showed that it was capable of detecting a threshold, among other forms on nonlinearity, with good accuracy and no bias. This held true even with measurement error in exposure. I then applied it to a study of air pollution and daily deaths in 10 U.S. cities. The figure below is the result, showing no evidence of a threshold down to the lowest levels of PM_{10}.

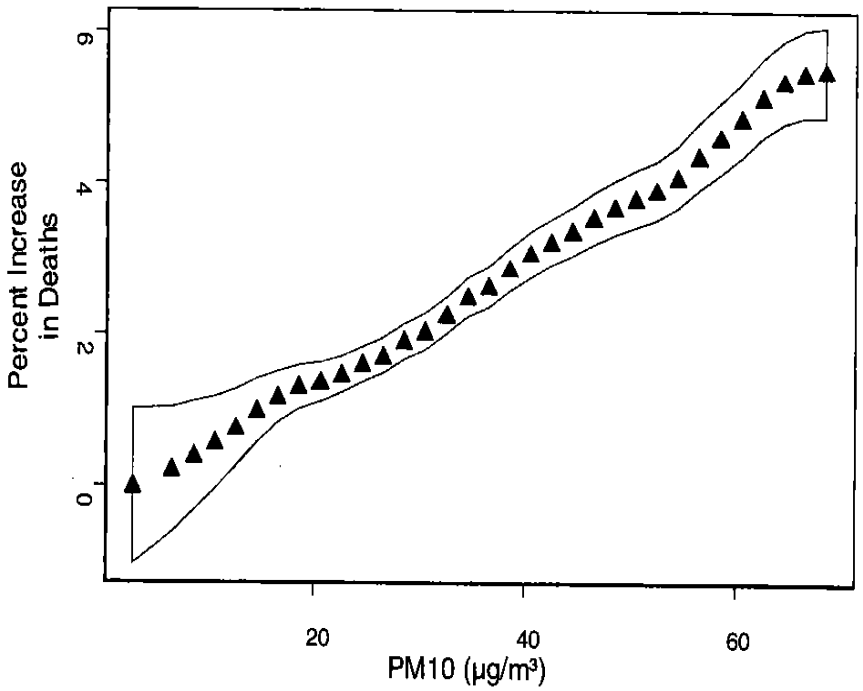
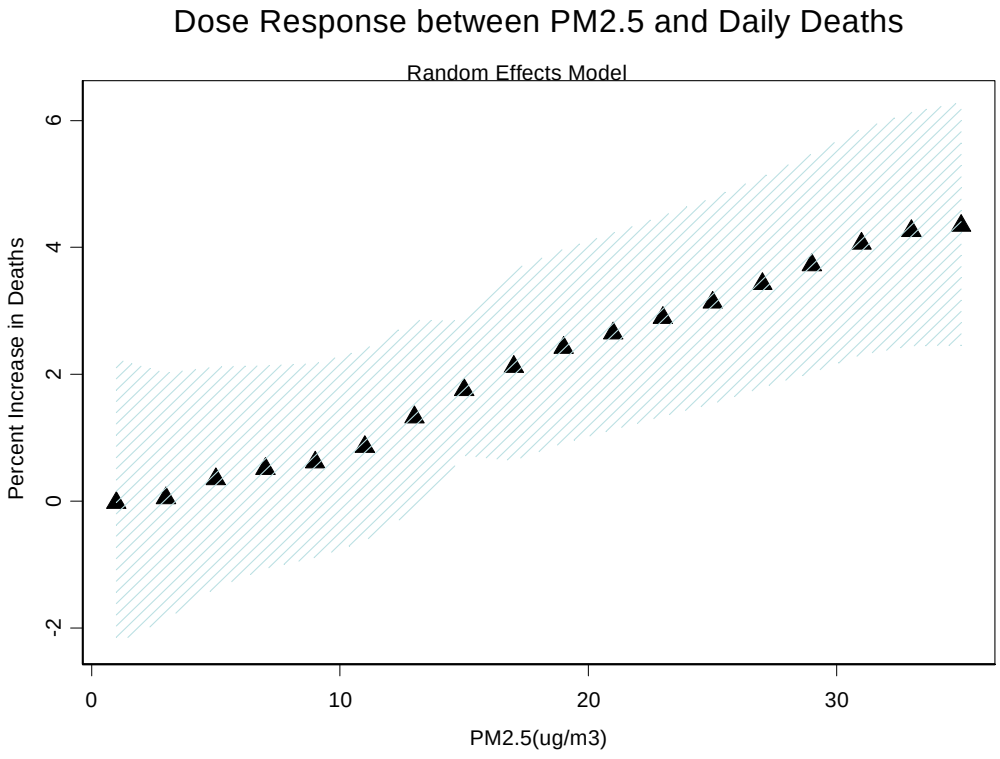


FIGURE 2. Dose response between PM_{10} and daily deaths in ten U.S. cities.

77. I also repeated this same analysis using $PM_{2.5}$ as the exposure, instead of PM_{10} in six U.S. cities where that data was then available. Those results are shown below. Note that essentially the entire dose-response curve takes place on days below the current ambient air quality standard.



Again, there have also been other approaches applied, again with the same conclusion .

Relationship with NAAQS

78. It is sometimes argued that by setting a National Ambient Air Quality Standard for particles EPA has explicitly determined that there are no adverse health effects at concentrations below that standard. EPA has explicitly rejected that interpretation. In its Regulatory Impact Analysis for the 1997 $PM_{2.5}$ standard EPA specifically rejected this view, stating that a NAAQS was not a "no effects" level. Specifically, they said, "The Act does not require the Administrator to establish a primary NAAQS at a zero-risk level". More recently, in its Regulatory Impact Analysis for the Clean Air Interstate Rule (2005) EPA stated that:

> The benefits estimates generated for the final CAIR are subject to a number of assumptions and uncertainties, which are discussed throughout this document. For example, key assumptions underlying the primary estimate for the mortality category include the following:
> 1) Inhalation of fine particles is causally associated with premature death at concentrations near those experienced by most Americans on a daily basis. Although biological mechanisms for this effect have not yet been completely established, the weight of the available epidemiological and experimental evidence supports an assumption of causality.
> 2) All fine particles, regardless of their chemical composition, are equally potent in causing premature mortality. This is an important assumption, because PM produced via transported precursors emitted from EGUs may differ significantly from direct PM released from automotive engines and other industrial sources. However, no clear scientific grounds exist for supporting differential effects estimates by particle type.
> 3) The C-R function for fine particles is approximately linear within the range of ambient concentrations under consideration. Thus, the estimates include health benefits from reducing fine particles in areas with varied concentrations of PM, including both regions that are in attainment with the fine particle standard and those that do not meet the standard.

79. Similarly, in the EPA Particulate Matter Staff Paper (EPA, 2005) EPA concluded that, "it is appropriate to use the linear or log-linear concentration-response models reported in epidemiologic studies in the quantitative risk assessment" (p 3-59).

The staff paper was reviewed and approved by EPA's external Clean Air Scientific Advisory Committee.

80. EPA is joined in its conclusion that the dose-response relation is linear with no evidence of a threshold by the National Academy of Sciences, which in two reports endorsed such a conclusion, and its use in estimating the public health benefits of controlling air pollution. Thus, in 2002, the academy stated, "For pollutants such as PM_{10} and $PM_{2.5}$, there is no evidence for any departure of linearity in the observed range of exposure, nor any indication of a threshold" (NRC 2002).

81. This is also consistent with EPA's Expert Elicitation Report, where 11 out of 12 reviewers believed there was neither evidence nor a theoretical basis for a threshold. The remaining reviewer thought there was a 50% probability of a threshold, but that if it existed, there was an 80% probability that it was below 5 $\mu g/m^3$. There are no counties in downwind states of the Monroe plant where annual average concentrations get that low, rendering such a threshold moot.

Implications of a Linear Relationship

82. If, as the data indicate, and the scientific community believes, there is a linear dose-response between mortality and $PM_{2.5}$ concentrations, then any increase in particle concentrations in downwind communities of a coal burning powerplant will result in an increase in the death rate in those communities. While the increased rate will depend on the amount of increase in particle concentrations, and in some cases may be low, it will not be zero. Hence, there will be early deaths associated with such an increase, over time.

Importance of $PM_{2.5}$

83. A number of studies have documented greater effects of $PM_{2.5}$ on mortality than of coarse particles. Most recently, we examined the association between $PM_{2.5}$, coarse mass (the difference between PM_{10} and $PM_{2.5}$, representing particles with sizes between 2.5 and 10 μM), and daily deaths in 112 U.S. cities. We found each 10 $\mu g/m^3$ increase in particles was associated with a 1 % increase in daily deaths, while coarse mass was associated with about half that increase.

Mortality Displacement

84. If the deaths occurring after acute exposure to PM were only being brought forward by a few days, they would have much less public health significance. This issue was discussed in the section on Chronic Exposure effects, since the opposite appears to be true—the number of particle-associated deaths seems to rise with time after exposure, rather than being compensated for by a period of fewer than expected deaths. Hence this is not an issue. This seems to be because, in the image below, the effect of air pollution on recruitment into the Risk Pool is greater than its effect on dying out of the risk pool. Hence instead of depleting the pool, air pollution increases it, leaving more vulnerable people to die in subsequent days.

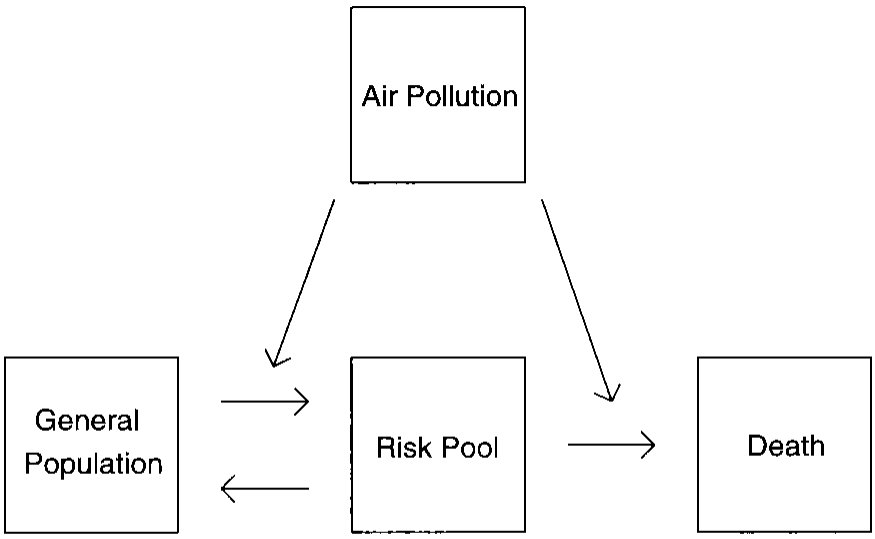


Fig. 1. The mechanics that lead to the mortality displacement.

Morbidity Studies

85. Particles in the air are not merely responsible for early deaths. They have a wide range of other heath effects, including triggering heart attacks, exacerbating respiratory infections to the point where the require hospitalization, triggering asthma attacks, etc. In the section below I briefly describe the evidence for some of these effects.

86. Hospital admission for heart disease and lung disease increase following increases in particles in the air. This has been demonstrated in numerous studies over the last several decades.

Respiratory Disease

87. Bates and Sizto first reported that sulfate particles from coal burning power plants were associated with hospital admissions for respiratory disease in Ontario back in the 1980's. Since that time, numerous studies have reported associations of particles and respiratory

admissions in Europe, the U.S. and Canada. These were followed by larger, multi-city studies that provided more stable estimates and made use of the same approaches described for the time series mortality studies to assure that associations were not confounded by other pollutants and temperature. In addition, several single city studies took advantage of special circumstances to rule out confounding. For example, I found that particles were associated with respiratory admissions in Spokane, WA, a town with essentially no SO_2, and where there was no correlation between particles and temperature, ruling those two out as potential confounders. I also showed that excluding very hot and very cold days, when one would expect the greatest effect of temperature, had no impact on the particle effects.

88. Hospital admissions for heart disease are also increased when particle concentrations go up. This is seen for all heart disease admissions, as well as for important categories of cardiovascular disease, such as heart attack, heart failure admissions, arrhythmia admissions, and strokes. For example, in a 1995 study in Detroit, I reported that heart attacks, as well as admissions for heart failure, increased as PM_{10} rose. Again, when I looked at a city where PM_{10} was essentially uncorrelated with SO_2 or Ozone, I found the same result. Studies such as these have again been followed by large multicity studies reporting associations with particles that are not confounded by other pollutants or weather.

Heart Attacks

89. The association of particles with an immediate increase in hospital admissions for heart attacks indicates that particles must be triggering the occurrence of heart attacks. There is considerable other evidence to suggest that is the case. First, studies have interviewed patients who survived heart attacks, and, using case-crossover analyses, found associations with particles.

Other focused studies had mixed results. However a large study of 21 U.S. cities definitively confirmed the association. A recent study examined emergency visits for acute coronary syndrome, essentially an early stage of a heart attack, and confirmed an association with particles (Lippi, 2009). Moreover, there is considerable toxicologic and mechanistic support for this effect. These are discussed below, under mechanistic studies.

Heart Failure

90. Heart failure is a serious disease where the heart's ability to pump blood to the body is impaired. Patients with heart failure have significantly reduced life expectancy, and episodes of increased impairment are dangerous, and frequently result in hospitalization. It is a large, growing, and expensive component of the nation's hospital burden. My study in 1995 identified increases in heart failure after increases in PM_{10} concentrations, indicating that particle exposure could cause an imbalance of the compensation that the body (with medication) makes for the poor pumping ability of the heart. Since then, those associations have been confirmed, including in large multi-city studies.

Stroke

91. The finding that particles increase strokes, a severely debilitating disease, was first reported in Asia. Recently, this has been confirmed in large multi-city studies in the U.S.. Interestingly, the association seems limited to ischemic strokes, not hemorrhagic strokes, which is consistent with the association with heart attacks.

IV.c. Mechanistic Studies

Oxidative Stress

92. Animal experiments indicate that reactive oxygen species (such as hydrogen peroxide, superoxide, etc), which have established relevance in the pathogenesis of cardiovascular disease and aging, are affected by particles, which represent one pathway for their cardiovascular and lung effects. For example, the figure below shows the increase in reactive oxygen species in animals within hours of exposure to concentrated particles from Boston air. Sulfate is one of the major contributors to Boston particles. Even more impressive, when animals who had been breathing Boston air (without concentration) were placed in a chamber where they could breathe filtered air, the concentrations of reactive oxygen species in the heart and lung fell by a third within days of removing the exposure (Figure 2). Moreover, it is evident from the figures that levels were still falling when the study was terminated.

Figure 1. Reactive oxygen species concentrations increase with PM Exposure

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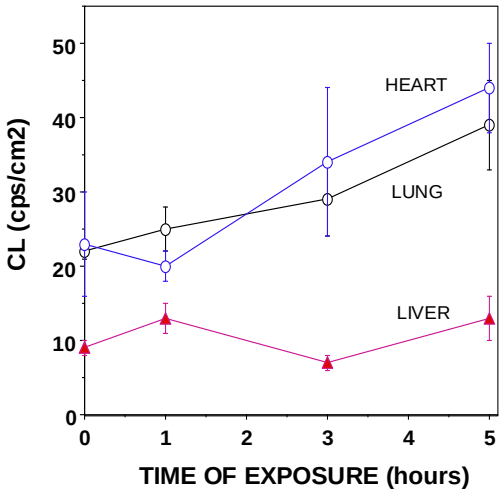
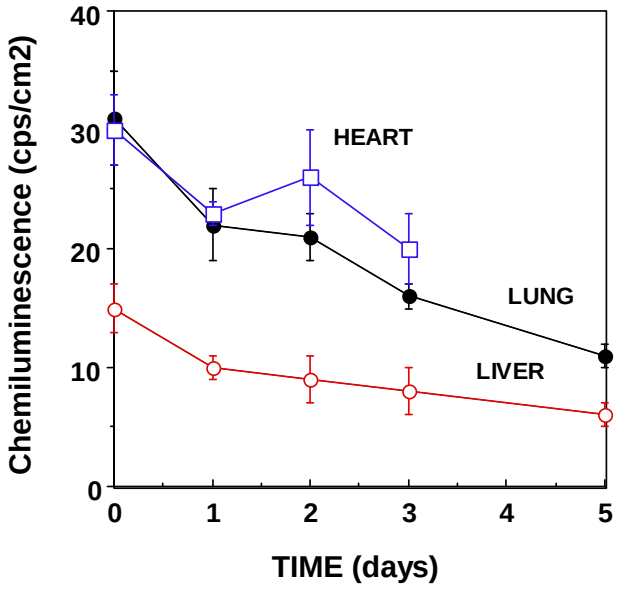


Figure 2. Reactive Oxygen Species decrease following removal of PM



93. Diesel particles have also been shown to increase oxidative stress in endothelial tissue, inducing the production of heme oxygenase-1, a rapid response part of the bodies defense system against oxidative stress. The viability of cell cultures of microvascular endothelial cells was impaired by diesel particles with an accompanying large increase in induction of heme oxygenase-1.

94. A series of studies have examined the role of genes related to oxidative stress on cardiovascular effects of particles, particularly heart rate variability (HRV). Schwartz and Chahine have reported that subjects that were missing the gene that makes glutathione S Transferase M1 (part of the defense against systemic oxidative stress), or with a variant of the *HMOX-1* gene that is less good at producing the antioxidant heme oxygenase, had larger effects

of particles on HRV, including a significant 3-way interaction. Other studies have focused on oxidative stress per se. For example, Rossner and colleagues examined bus drivers in Prague, and reported increased levels of indicators of oxidative stress such as F-2 isoprostane and 8-OHdG in drivers compared to controls.

Inflammation

95. Particles in the air have been shown to induce increases in inflammation in the lung, as well as systemically (which affects the heart). For example, exhaled NO is a marker for inflammation in the lung. Several studies have shown that particles increase exhaled NO in both children and the elderly. The urinary excretion of 8-hydroxy-2′-deoxyguanosine (8-OHdG) often has been used as a biomarker to assess the extent of repair of DNA damage (induced by inflammation and oxidative stress) in both the clinical and occupational setting. Particles, and particularly the metals on particles, have also been associated with an increased production of 8-OHdG, including specifically exposure to traffic pollution. 8-OHdG was also elevated in urban children compared to rural children.

96. CRP, ICAM-1, VCAM-1, and homocysteine are blood markers of the interrelated processes of inflammation and endothelial function, which play important roles in heart disease and atherosclerosis. Accordingly, CRP, ICAM-1, VCAM-1, and homocysteine have been shown to be independently and jointly associated with increased cardiac risk. In a prospective study of 28,263 healthy, post-menopausal women, for example, increased CRP and ICAM-1 were associated with increased risk of cardiac events. Correspondingly, elevated levels of ICAM-1 were associated with the development of accelerated atherosclerosis in a case-control study of 14,916 middle-aged men, while VCAM-1 predicted hospital events in angina patients[160]. Homocysteine, which inhibits NO release, has also been associated with coronary artery disease

measured radiographically and with flow mediated dilation. Hence examining these markers in response to air pollution is important. Particles have been shown to increase sICAM-1 and sVCAM-1 in diabetics, a finding confirmed in a controlled human exposure chamber study. Particles associations with CRP have been mixed in studies, but the effect may be limited to the obese or diabetics. Particles also increase homocysteine in the elderly.

97. Inflammation can also inhibit immune defenses against infections, and animals infected with Strep pneumonia and exposed to concentrated particles showed substantial worsening of the infection compared to control animals breathing filtered air.

Coagulation/Thrombosis pathway

98. Both animal and controlled human exposure studies have demonstrated that ambient particles can increase pro-thrombotic (i.e. clot forming) activity and even induce thrombosis in acute exposures. Thrombosis is associated with a range of adverse outcomes including embolisms, heart attacks, and, on a chronic basis, increased atherosclerosis. There is recent epidemiology that supports this finding. Baccarelli and coworkers reported an association of airborne particles with decreased clotting time, as well as the risk of deep vein thrombosis. This is consistent with the results of a controlled exposure study to Diesel particles, which reported increased ST depression (the depression of the ST segment of an electrocardiogram, which is a sign of ischemic heart disease) and alterations in fibrinolytic capacity (the ability to break up clots that have formed in blood vessels). Further support comes from a recent study of almost 58,000 women in the Women's Health Initiative. They found that $PM_{2.5}$ was associated with a 4% increase in the risk of an ST abnormality on the electrocardiogram and a 5% increase

in the risk of a T wave abnormaility (Zhang 2009). In addition, Kuenzli et al have reported an association of particle exposure with chronic atherosclerosis.

99. Suwa et al. have demonstrated that exposure to particles increases plaque formation and decreases plaque stability. Other studies have also indicated that enhanced throbosis in animals exposed to particles. Such changes increase the risk of a heart attack.

Ischemia

100. A number of studies have directly linked particle exposure with ischemia (reduced blood supply to the heart). Wellenius exposed dogs to either filtered air or concentrated air particles, followed by a temporary occlusion of the coronary artery. The animals exposed to particles experienced greater ischemia than those exposed to filtered air. Similarly, human volunteers exposed to particles manifested myocardial ischemia, and impaired ability to dissolve clots. And a follow-up study of a registry of patients who underwent coronary artery catherization in Utah found an association between particles and ischemic events. A standard measure of ischemia derived from electrocardiogram patterns is ST segment depression. Recent studies of subjects undergoing repeated examinations have found that particles are associated with increases in ST segment depression in vulnerable populations. This was also seen in human volunteers experimentally exposed to particles.

Blood Pressure Changes

101. Elevated blood pressure (BP) predicts cardiovascular morbidity and mortality, including heart attacks, and reductions in BP have been shown to reduce risk. Several studies have observed positive associations between ambient air pollutants and BP, although other

studies have failed to find associations or have even detected inverse associations between ambient air pollutants and BP.

102. There is evidence of both immediate effects and delayed effects over several days. Providing a mechanistic link relating particles to blood pressure, endothelin-1, which modulates systemic vascular tone, is known to increase in response to reactive oxygen species, which are elevated by particles (as noted above), and endothelin-1 has also been shown to increase directly in response to urban PM. Li and colleagues found that losartan, an antagonist of angiotensin II type 1 receptors, inhibits the vasoconstriction effect of urban particles on human pulmonary artery endothelial cells. In addition to its effects on blood pressure, angiotensin II is also a proinflammatory mediator, raising the possibility that the local renin–angiotensin system and systemic inflammation may be interrelated components of the cardiovascular system's response to ambient particles and the oxidative stress they induce.

103. Controlled human exposure studies have recently indicated that airborne particles are associated with acute changes in blood pressure. One study reported an association between arterial diameter and particle exposure. A follow-up study reported a direct association with blood pressure. This is supported by observational epidemiology studies in panels of subjects in Germany and the US. A more recent study (Wilker, 2009, looked at the change in blood pressure from sitting to standing, and found $PM_{2.5}$ was associated with these changes, and the effects were modified by genes related to pathways of blood pressure control. However the most exciting development in this field is one of the few uses of a randomized controlled trial in environmental epidemiology. McCracken and coworkers randomized houses in rural Guatemala that initially used unvented open fires for cooking to either receive a chimney stove (treatment group) or not (control group). Women over age 45 who cooked were examined in both groups, and a

significantly lower blood pressure was found in the intervention group[199]. At the end of the trial, the control group was given the same stove, and the investigators returned to measure blood pressure in the controls, using a pre-post design. Again, stove intervention was associated with a reduction in blood pressure.

Electrical control of the Heart

104. One potential pathway for the cardiovascular effects of particles is to change the autonomic nervous system, which affects both blood pressure, and the electrical control of the heart. The lung contains nerve endings from the autonomic nervous system, and stimulation or irritation of these nerve endings has been shown to have cardiovascular effects. One measure of such effects is from studies that have looked at repeated visits of subjects with electrocardiograms measured at each visit. Electrocardiogram changes in these studies have been related to particles in the air. Moreover, animal studies, and controlled human exposure studies, have confirmed such results. These studies are important because the types of electrocardiogram changes associated with particle exposure have been shown to increase the risk of death. Note that this applies to both short term and long term changes in these patterns.

Endothelial Pathway

105. The endothelium is the lining of the arteries, and it is not merely the coating of a tube carrying fluid. It is biologically active. When stressed, endothelial cells can activate clotting mechanisms, recruit inflammatory cells, which can disturb atherosclerotic plaques that have previously formed, and impair clot dissolving functions. Acutely, these can result in ruptures of the plaques, which trigger heart attacks; more chronically, it can result in atherosclerosis. Particles in the air affect these things. For example, Suwa and coworkers showed in animal

models that particles increase the rate of growth of plaques, and decrease stability—increasing the risk of a rupture. In general, indicators of endothelial dysfunction have been shown in epidemiologic, toxicologic, and controlled human exposures. These finding are quite consistent with the findings that particles are associated with heart attacks and sudden deaths.

106. Another recent study of mice genetically prone to atherosclerosis and on a high fat western diet exposed to concentrated particles from the outside air showed that the particle exposure lead to more atherosclerotic plaque, and increased macrophages and tissue factor in the plaques, which reduce plaque stability and increase the risk of a heart attack. An earlier study, in the northern suburbs of New York, where sulfates from coal burning power plants are a major fraction of the particles, again reported increased plaque and increased vasoconstriction in mice genetically prone to atherosclerosis. A more recent study, using a different mouse model of atherosclerosis documented that particle exposure increased oxidation of LDL (making it much more dangerous), increased the thickness of the arterial wall, and promoted plaque growth and instability. Yet, another study looked at gene expression in arterial tissue of animals following exposure to filtered air or particles. They reported clear signs of hundreds of genes changing their expression pattern after particle exposure, including increases in the inflammatory and cell proliferation (needed to thicken arterial walls and grow plaque) pathways.

V. SULFATES

107. While the association between exposure to particulate matter (PM) mass and mortality is well established, there remains uncertainty as to whether certain chemical components of PM are more harmful to human health than others. To date the evidence is not convincing that any form of fine combustion particles are more or less toxic than average, with

different studies showing different results. It is important to understand that the conclusion (of the Clean Air Scientific Advisory Committee and others) that we cannot differentiate the toxicity of different types or sources of particles does not mean that we believe it likely that one type of source of particles will ultimately prove to be the "toxic agent". Rather, the consensus scientific opinion is that all fine combustion particles are toxic, although they may vary in their toxicity. There have been time series studies in locations, such as Santa Clara, CA, in the winter, where wood smoke is the dominant source of particles, that show significant associations with daily deaths. There are studies in locations such as Philadelphia where secondary sulfate particles are the major source, which again show day to day changes in air pollution are associated with day to day changes in deaths. In Sao Paolo, Brazil, where traffic particles are the major sources, again, particles are associated with increased deaths. While we have not yet distinguished the relative effects of different sources of particles, it is clear that they all contribute to early deaths.

108. In the absence of good evidence that any source or type of particle had a *different* impact, CASAC recommended maintaining a standard for $PM_{2.5}$, that is, treating particles from all sources as having the *same* toxicity.

109. Sulfates are the principal particle type generated by coal burning power plants. Cohort studies such as the Six City Study and the ACS Cohort have reported that sulfates were associated with decreases in long term survival.

110. Sulfates have also been associated with increases in mortality in time series studies of acute exposure, including Mar et al who found increased total and cardiovascular mortality associated with a regional sulfate factor in Phoenix, suggesting that the impact of sulfates is not only an east coast phenomenon. While epidemiologic studies generally do not have the strength of an experimental design, the study of Pope and coworkers is an exception to

that rule. They looked at a natural experiment. A copper smelter strike in the Southwest between 15 July 1967 and early April 1968 shut down all the smelters in the region. During that period, smelters accounted for the large majority of the sulfate particles in these southwestern states. As reported by Trijonis and Yuan (1978) and Trijonis (1979) this strike led to significant reductions in sulfate particles in the Southwest, with an average decrease of 60% during the 8.5 month strike, which was equivalent to a reduction of approximately 2.5 $\mu g/m^3$ in mass concentration. This natural experiment really is equivalent to a randomized trial. The population of the downwind states had no choice in the matter—they were exposed to higher, lower, and higher sulfate concentrations over time, just as in a crossover trial for a drug. Nor did they even have a perception that their exposure was changed, since sulfate concentrations are not a routinely monitored criteria air pollutant, and there was little public attention to air pollution in this period.

111. Pope and coworkers analyzed this natural experiment to see how mortality rates change in response to the change in sulfate concentrations. After controlling for time trends, mortality counts in bordering states, and influenza/pneumonia deaths, they found that the 2.5 $\mu g/m^3$ decrease in sulfate particle concentrations resulted in a 2.5% decrease in the number of deaths in the four-state region. This unambiguously establishes secondary sulfate particles as a cause of early death.

112. In comparison, a 2.5 $\mu g/m^3$ decrease in long term average $PM_{2.5}$ concentrations in the American Cancer Society Cohort study was associated with about a 1.5% decrease in deaths, whereas in the Harvard Six City Cohort, the same decrease was associated with a 4% reduction in deaths. Hence this natural experiment not only shows that sulfate particles kill people, its effect size is consistent with the long term studies of mortality from following cohorts. This has two implications. First, it again suggests that there is no reason to believe that sulfate particles

are less toxic than average. Second, it shows that the reductions in mortality from reducing air pollution do not take years to show up, they occur within the first year. If additional reductions would have occurred in subsequent years, then this study underestimates the health benefits of reducing sulfate particle levels.

113. Although Schlesinger noted that many toxicological studies of simple artificially generated sulfate particles have not found a significant biological response, O'Neill et al found an association between real outdoor sulfate particles and endothelial dysfunction, and Chuang found sulfate increased oxidative stress and coagulation in a panel study. Sulfate particles were also associated with disturbances in electrocardiogram patterns in studies of repeated measurements in two different populations of elderly adults. The positive sulfate effects observed in epidemiological studies may be attributable to the greater complexity of the sulfate particles in ambient air than the simple ammonium sulfate often used in toxicological studies. For example, acid sulfate in the form of sulfuric acid or ammonium bisulfate can convert insoluble metal oxides (also present in ambient particulate pollution) to bio-available sulfate salts, and studies of particles collected in Washington DC have shown that much of the metal content was associated with sulfates. Metals on particles in turn have been linked to a wide variety of toxic responses. For example, toxicologic studies show Zinc sulfate to have cardiotoxicity. Other toxicologic studies have shown that sulfate particles produce lung inflammation and increased clotting factors in the blood.

114. Recently, Franklin and coworkers used data from the PM speciation network to examine this question further. Because particle components, including sulfates, were only monitored 1 day in 3 or 1 day in 6, while $PM_{2.5}$ was monitored daily, they used a two stage approach. Taking advantage of the natural variation in PM components between cities, and

between seasons within city, they fit season specific regressions in each of 25 cities with speciation monitors, in each season. In a second stage, they examined how the association between $PM_{2.5}$ and daily deaths was modified by the ratio of sulfate to particle mass, and similarly for the other measured components. If sulfates have a different toxicity than average for particles, then one would expect that a city where a high fraction of total particles were sulfate would have a different slope than a city with a low fraction. We found a significant overall effect of $PM_{2.5}$ with all cause mortality. Cities with high fractions of sulfate, arsenic (also a tracer of particles from coal burning power plants), silicon, and nickel had roughly twice the mortality slope as cities with low fractions. When multiple components were considered simultaneously, sulfate, nickel, and aluminum remained significant, and explained all of the apparent variation in effect estimates across cities and seasons.

115. A new analysis of the ACS study by Krewski and coworkers examined the extended follow-up period for the ACS, and looked at sulfate particles as well as all PM2.5 (Krewski D, Jerrett M, Burnett RT, et al. Extended follow-up and spatial analysis of the American Cancer Society study linking particulate air pollution and mortality. Research report (Health Effects Institute) 2009(140):5-114; discussion 5-36.) Interestingly, they found a stronger effect for sulfates. They report that after controlling for the maximum number of individual and area based potential confounders the hazard ratios for sulfates were 1.045 if they used as exposure sulfate levels two years before the cohort was recruited, and 1.086 when they used sulfate levels from 1990, roughly the midpoint of the follow-up of the cohort. These hazard ratios were for a 5 μg/m3 increase in sulfate levels, and correspond to 9% and 17% increases in deaths per 10 $\mu g/m^3$ respectively.

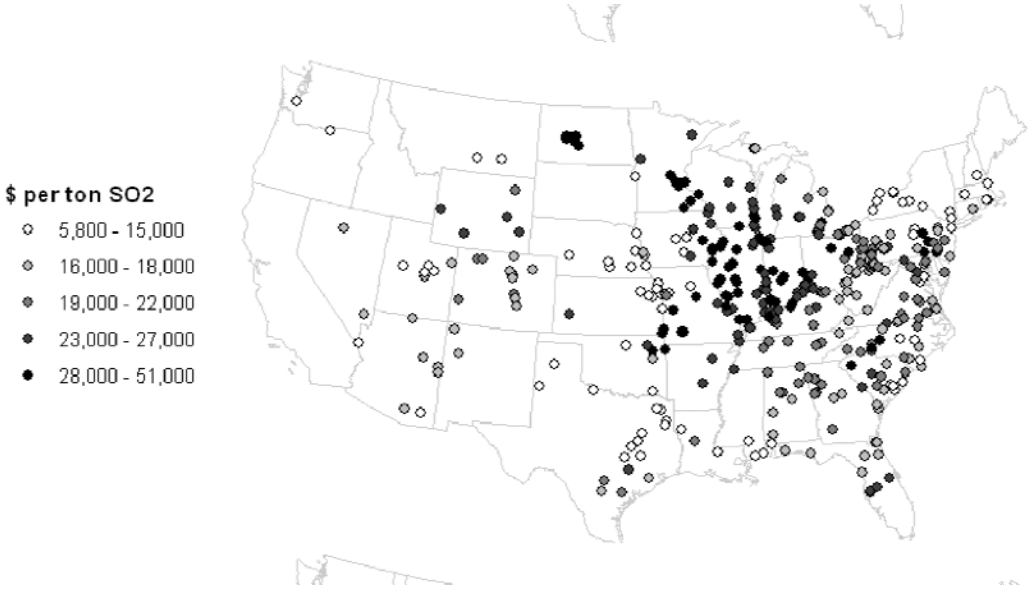
VI. QUANTITATIVE RISK ASSESSMENT

116. We have recently published a peer reviewed, quantitative risk assessment and benefit analysis for 407 coal burning power plants in the US (Levy 2009). We assessed the impact of emissions from 407 coal burning powerplants in the United States on health in every county of the United States, using emissions data for 1999. From that, we estimated the increase in deaths in each county, using the dose-response relationship from Schwartz (2008). We valued those deaths at the median of the estimates of a value of a statistical life, which we took to be $6 million per death.

117. This estimate is not really a price on a life. It is obtained by estimating how much people are willing to pay for small reductions in their risk of death, and converting. So if people are willing to pay $X for a reduction in risk of 1 in 10,000, than reducing risk in enough people to produce, on average, 1 fewer deaths would be worth 10,000 X dollars. This estimate is based on research where people are asked how much they would pay for consumer products that reduce risk or alternatively, examine how much more employers have to pay employees (adjusting for age, education, experience, etc) to compensate for taking an increased risk of accidental death.

118. To make these results more useful for policy purposes, we converted them into the costs per ton of SO_2 emitted, or alternatively, the cost per kilowatt hour of electricity produced. We also estimated uncertainties around these estimates, incorporating uncertainties for the modeled exposure estimates, uncertainties around the dose-response curve, and uncertainties in the value of a statistical life. A primary goal of our paper was to estimate how variable the damages from emissions were from plant to plant in the US. We found a median estimate of $19,000 per ton SO2 emitted, but substantial geographic variation. In general tons of SO2 emitted in Midwestern states caused more damage, since there was a greater population

downwind. This is shown in the figure below. Power plants in the Detroit area had particularly large damages per ton.



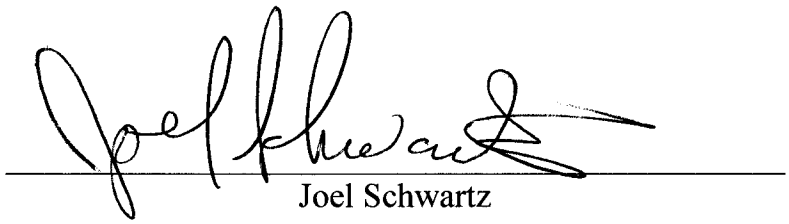
119. For NOX emissions the median damage per ton of emissions was $4,800, again with higher damages from the Industrial Midwest.

120. If we ignore the higher damages than average that likely result from emissions at the Monroe plant, we can estimate the total damage of the excess emissions using the median values. Using that conservative approach, and taking the annual excess emissions from Monroe 2 as 26,525 tons of SO2 and 7942 tons of NOX, then I project those emissions will result in $542 million in damages per year. This level of excess emissions would be expected to result in an additional 90 deaths per year in the downwind area. Thus eliminating that number of emissions would save 90 lives per year and save $542 million in social costs.

VII. CONCLUSIONS

121. In summary, particles in the air are associated with large numbers of deaths, heart attacks, hospitalizations for pneumonia, and other serious health impairments. There is no evidence for a threshold for these effects, which means that any incremental exposure is associated with incremental deaths, heart attacks, etc. in the general population. Coal burning power plants are a major source of these particles, and there is conflicting evidence on whether the particles from this source are more or less toxic than average, with the most recent data suggesting higher than average toxicity. Hence any emissions from these power plants caused serious harm to human health, including early deaths, and any reduction in emissions will have health benefits. Eliminating the excess emissions from this plant would result in approximately 90 fewer deaths per year in the exposed area, which, if this occurred in an occupational setting, would save an additional $540 million in wages to convince the workers to continue employment.

I declare under penalty of perjury that the foregoing is true and correct.



Joel Schwartz

Executed on July _21, 2010 in Boston, Massachusetts

ATTACHMENT A – CURRICULUM VITAE/RESUME AND LIST OF PUBLICATIONS

CURRICULUM VITAE

NAME:	JOEL SCHWARTZ
ADDRESS:	207 Lincoln Street, Newton Highlands, MA
PLACE OF BIRTH:	New York, New York
EDUCATION:	1969 B.A. Brandeis University
1980 Ph.D.	Brandeis University (Theoretical Physics)

ACADEMIC APPOINTMENTS:

2005 to present	Professor of Environmental Epidemiology, Harvard School of Public Health Director, Harvard Center for Risk Analysis
1994 -2004	Associate Professor of Environmental Epidemiology, HSPH
1994 - present	Associate Professor of Medicine, Harvard Medical School
1991-93	Lecturer, Department of Environmental Health, Harvard School of Public Health

HOSPITAL APPOINTMENTS:

1994 -	Associate Epidemiologist, Brigham and Women's Hospital

OTHER PROFESSIONAL POSITIONS AND MAJOR VISITING APPOINTMENTS:

1977-79	Legislative Assistant for Energy and Environment, Congressman Timothy Wirth
1979-87	Staff Scientist, U.S. Environmental Protection Agency
1987-88	Visiting Scientist, Department of Biostatistics, Harvard School of Public Health
1989, 94	Visiting Scientist, Department of Social and Preventive Medicine, University of Basel, Switzerland
1990	Visiting Scientist, Department of Occupational Safety and Environmental Health University of Wuppertal, Germany
1989-93	Senior Scientist, U.S. Environmental Protection Agency

HONORS AND DISTINCTIONS:

2008	John Goldsmith Award, International Society for Environmental Epidemiology Nichols Teaching Award, Harvard School of Public Health
2001	International Union of Environmental Protection Agencies World Congress Award
1999	Twentieth Century Distinguished Service Award, Lukacs Symposium for Statistical Ecology and Environmental Statistics
1991	John D and Catherine T MacArthur Fellowship
1984, 86	U.S. Environmental Protection Agency Silver Medal
1988, 89, 90, 92	U.S. Environmental Protection Agency Scientific Achievement
1991	Alumni Achievement Award, Brandeis University

MAJOR COMMITTEE ASSIGNMENTS:

National

1985	Preventing Lead Poisoning in Young Children document, Consultant, Centers for Disease Control
1988	Advisory Committee, Boston Soil Lead Study
1989-92	EPA Environmental Health Review Panel, Environmental Protection Agency
1989-93	National Academy of Science, Committee on Assessing Lead Exposure in Critical Populations
1990-93	National Academy of Science, Committee on Environmental Epidemiology
1992	Advisory Committee, Resources for the Future Center for Risk Management, Public Health/ Environmental Health Risk Studies
1992	Environmental Epidemiology Advisory Committee, Pew Memorial Trusts
1992	Ethics Committee, International Society for Environmental Epidemiology
1992	Reviewing Committee, Office of Technology Assessment for Identifying and Controlling Pulmonary Toxicants
1992-present	Technical Advisory Committee, Alliance to End Childhood Lead Poisoning
1992	Technical Advisory Committee, New York State Environmental Externalities Cost Study
1993	Subcommittee on Lead, National Advisory Committee on Environmental Policies and Technology
1993-present	Research Advisory Committee, National Center for Lead Safe Housing
1994-2002	Center for Disease Control, Advisory Committee on Childhood Lead Poisoning Prevention
1994-2005	Mickey Leland National Urban Air Toxic Research Center, Scientific Advisory Panel Environmental Statistics Subcommittee, National Advisory Committee on Environmental Policy and Technology
1998	Franklin Institute Science Medal Prize Committee
2003-2005	HSPH Disciplinary Committee
2004-present	Steering Committee, Harvard University Committee on the Environment
2005	EPA Science Advisory Board, Ad Hoc All Ages Lead Committee
2005-2008	Councilor, International Society for Environmental Epidemiology
2005-present	Editorial Board, American Journal of Respiratory and Critical Care Medicine
2005-2008	EPA Lead Clean Air Science Advisory Committee
2008-2009	EPA Board of Scientific Councilors, Human Health Subcommittee

International

1993-2004	European Economic Community Studies on Air Pollution, Daily Mortality, and Hospital Emergency Visits, Advisor
1993	Advisory Committee, European Economic Community Panel Studies Air Pollution, Pulmonary Function, and Respiratory Function
2000-2004	Chair, Statistics Advisory Committee, APHEIS Project

PROFESSIONAL SOCIETIES

1987	American Statistical Association
1988	American Thoracic Society
1990	Society for Epidemiologic Research
1991	International Society for Environmental Epidemiology

Editorial Board

	Epidemiology Editor, International Journal of Biometeorology
2005-present	Editorial Board, American Journal of Respiratory and Critical Care Medicine

MAJOR RESEARCH INTERESTS:

1. Respiratory Epidemiology
2. Air, Water and Lead Epidemiology
3. Epidemiologic Methods
4. Cost-Benefit Analysis

TEACHING EXPERIENCE:

1992	Environmental Epidemiology Course, University of Basel @ 30-40 Graduate Students 120 Preparation Time each year, 35 class hours
1994, 97, 99, 2009	Advanced Topics in Environmental Epidemiology, University of Basel, @ 20 Graduate Students, 35 class hours
1995	Short Course on Advanced Regression Analysis in Environmental Epidemiology, San Miniato, Italy @ 23 Graduate Students, 35 class hours
1996–present	Professor, ID 271 HSPH, joint course on Advanced Regression Analysis for Departments of Epidemiology, Environmental Health, and Biostatistics, 21 Graduate Students, 35 class hours
2007-present	Professor, EH520 Seminar on preparing research proposals
2007-present	Environmental Epidemiology, Cyprus International Institute
2009-present	Professor, Epi204-Analysis of Case Control and Cohort Studies
	European Course on methods for Poisson Time Series, Santorini Greece, @40 Graduate Students, 35 hours

	Short Course on Advanced Regression in Environmental Epidemiology, Annual meeting of International Society for Environmental Epidemiology, 45 Graduate Students, 7 hours
	European Course on methods of Meta-analysis. Santorini Greece, 40 students, 24 course hours
2006	Environmental Epidemiology, National Institute of Public Heath, Mexico 40 students 30 hours